

21/ Declaration

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: H. MURAD

Application No.: 09/501,217

Art Unit: 1615

Filed: February 10, 2000

Examiner: L. S. Channavajjala

For: FRUIT EXTRACT COMPOSITIONS FOR
TREATING DERMATOLOGICAL
DISORDERS

Atty Docket No.: 2267-017

DECLARATION OF DR. HOWARD MURADAssistant Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

I, Howard Murad, inventor of the above-identified application, hereby declare that:

1. I am a citizen of the United States and reside at 4265 Marina City Drive, Penthouse 11, Marina del Rey, California 90292.

2. I have over 30 years experience in the field of dermatology and skin care and consider myself to be one of ordinary skill in the field. A copy of my *Curriculum Vitae* is attached hereto.

3. I am providing this declaration in support of the claims in the above-identified application in response to the Office Action mailed on August 28, 2003 ("Office Action"). I have read and understand the Office Action along with the references cited including U.S. Patent Number 5,985,300 to Crotty ("Crotty"), U.S. Patent Number 5,891,440 to Lansky ("Lansky"), and U.S. Patent No. 5,169,630 to Okaya ("Okaya"). Further, I have read and understand the claims presently at issue. The application describes and claims, *inter alia*, compositions for managing a dermatological condition in a patient which comprises at least one fruit extract from pomegranate; a hydrophilic moisturizing agent; a hydrophobic moisturizing agent; a mono- or poly-hydroxy acid; a pharmaceutically acceptable carrier and either a fruit extract from pomegranate and manganese ascorbate (claim 1); a fruit extract from pomegranate and copper sebacate (claim 28); a fruit extract from pomegranate and a manganese compound, a copper compound, or a selenium compound in an orally administered formulation (claim 33); a fruit extract from pomegranate (claim 33); or a fruit extract and a transition metal component (claim 35).

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4. In my clinic I have had the opportunity to study and compare the efficacy of compositions that include the combination of a hydrophilic moisturizing agent, a hydrophobic moisturizing agent, a mono- or poly-hydroxy acid, a pharmaceutically acceptable carrier, and at least one fruit extract from pomegranate (*i.e.*, the components of the composition of claim 34 of the invention) against the efficacy of these components individually for managing dermatological conditions. In my clinic I have observed that the combination of these ingredients is superior at managing dermatological conditions compared to either of the components individually. A composition comprising a combination of a hydrophilic moisturizing agent, a hydrophobic moisturizing agent, a mono- or poly-hydroxy acid, a pharmaceutically acceptable carrier, and at least one fruit extract from pomegranate, appears to act synergistically to more effectively manage dermatological conditions. Appendix A, attached hereto, provides two case studies for patients that I have treated in my clinic. Each of these case studies, which are representative of my clinical observations, shows that, when applied to a patient's skin for to treat a dermatological condition, a composition comprising at least one fruit extract from pomegranate in combination with a hydrophilic moisturizing agent, a hydrophobic moisturizing agent, a mono- or poly-hydroxy acid, and a pharmaceutically acceptable carrier is superior at managing the dermatological conditions compared to a composition comprising at least one fruit extract from pomegranate and one of a hydrophilic moisturizing agent, a hydrophobic moisturizing agent, or a mono- or poly-hydroxy acid. This improved efficacy was completely unexpected.

5. Thus, it is my professional opinion and conclusion that the claimed compositions for managing dermatological conditions that comprise the combination of a hydrophilic moisturizing agent, a hydrophobic moisturizing agent, and a mono- or poly-hydroxy acid; a pharmaceutically acceptable carrier; and either a fruit extract from pomegranate and manganese ascorbate (claim 1); a fruit extract from pomegranate and copper sebacate (claim 28); a fruit extract from pomegranate and a manganese compound, a copper compound; or a selenium compound in an orally administered formulation (claim 33); a fruit extract from pomegranate (claim 33); or a fruit extract and a transition metal component (claim 35) provides a surprising and unexpectedly beneficial effect that was not disclosed or suggested in the cited art.

6. I further declare that all statements made herein of my knowledge are true and all statements made on information and belief are believed to be true; and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of this application or any patent issuing thereon.

Dated this 10 Day of October, 2003.

Howard Murad M.D.
Howard Murad, M.D.

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CURRICULUM VITAE HOWARD MURAD, M.D.**Business Address:**

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El Segundo, CA 90245-4746

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(310) 335-1700 and (320) 726-3340

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(310) 335-1701

Birthdate:

4-18-39

Specialty:

Dermatology

EDUCATION:

1958-1962

Long Island University
BS in Pharmacy

1962-1966

University of California, Irvine
MD Degree

1963-1966

Practicing Pharmacist while attending medical school

1966-1967

Long Island Jewish Queens Hospital Center Rotating
Internship

1967-1969

General Medical Officer, U.S. Army

1969-1972

UCLA Wadsworth VA Hospital
Dermatology Residency

1972-1996

Private Practice, Los Angeles, CA

1996-Present

Private Practice, El Segundo, CA

1974-Present

Dermatology UCLA
Assistant Clinical Professor of Medicine

1990-Present

1. Founder of Murad Skin Research Laboratory
2. Product development in Skin Care
3. Involved in independent clinical research
4. Optimal Health Center – El Segundo for enhancement of life style – including nutrition and topical agents

LICENSURE:

California (G17115)

REGISTERED PHARMACIST: 1963

BOARD CERTIFICATION: The American Board of Dermatology
9-12-73

The American Board of Dermatology and The American
Board of Pathology
11-21-76

**ARTICLES, PRESENTATIONS
& PUBLICATIONS:**

Murad H, Moy LS. Use of AHA's add new dimensions to chemical peeling, Cosmetic Dermatology, May 1990

Moy LS, Murad H, Moy RL. Glycolic acid treatment on the facial skin, submitted Amer Facial Cosmet, 1992

Moy LS, Murad H, Moy RL. Procedures in treatment with glycolic acid, submitted to Internat J Dermatol, 1992

Murad H, Shamban A, Moy LS, Moy RL. Study shows that acne improves with glycolic acid regimen, Cosmetic Dermatology, November 1992

Murad H, Shamban A, Moy LS. Glycolic Acid for the treatment of polka-dot syndrome, Cosmetic Dermatol, March 1993

Moy LS, Murad H, Moy RL. Glycolic Acid peels for the treatment of wrinkles and photoaging, J Dermatol Surg Oncol, March 1993

Moy LS, Murad H, Moy RL. Glycolic Acid Therapy: Evaluation of efficacy and techniques in treatment of photodamage lesions, The American Journal of Cosmetic Surgery, 1993.

Murad H. Free Radicals and Antioxidants in Dermatology, Cosmetic Dermatology, October 1994

Murad H, Shamban A. Alternative Uses of Glycolic Acid, Cosmetic Dermatology, October 1994

Murad H, Shamban A. Various Combinations of Peeling Agents Improve Results, Cosmetic Dermatology, October 1994

Murad, H. The Use of Glycolic Acid as a Peeling Agent, Dermatologic Clinics, April 1995

Murad, H. "Indications, Techniques, Complications, and Alternatives to Chemical Peels of the Eyelids and Periorbital Area." Principles and Practice of Ophthalmic Plastic and Reconstructive Surgery, April 1995

Moy, LS, Murad, H, Moy, RL. Superficial Chemical peels, Cutaneous Surgery, Wheeland, 1994

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- Murad, H, Premo, PS. "Glycolic Acid: The Percentages Debate"
- Murad, H. "New Approach to Treating Facial Pigmentation"
- Murad, H. "Chemical Peels: Putting Your Best Face Forward"
- Murad, H. "Melasma – Some New Tools for Dealing with an Old Problem"
- Murad, H. "Look Again; It May Be Rosacea"
- Murad, H. "Acne Update: Cause and Treatments"
- Murad, H. "Seborrheic Dermatitis"
- Murad, H. "Melanoma Skin Cancer"
- Murad, H. "Maturing Skin"
- Murad, H. "Are you a victim of environmental aging?"
- Murad, H. "Increases in the incidence of skin cancer anticipated due to depletion of ozone layer"
- Murad, H. "Dysplastic Nevii: Helpful Early Warning Signs of Increased Melanoma Risk"
- Murad, H. "Urticaria Causes, Manifestations, and Treatments"
- Murad, H. "Advances in Liposomal Delivery Systems"
- Murad, H. "The Nails: Their Function and Care"
- Murad, H. "Tips for Prettier Hands and Feet."
- Murad, H. "Sunscreen Sense; Helping Each Client Select What's Best"
- Murad, H, Premo, PS. "Understanding Special Denatured Alcohol (SDA)"
- Murad, H. "Making the Best of Menopausal Skin"
- Murad, H, Murad M, Murad, H. "Basal Cell Carcinoma"
- Murad, H, Premo, PS. "Cell Turnover"
- Murad, H. "You are what you eat: diets, eating disorders and your skin"
- Murad, H. "How Deep is Skin Deep? The Basics of Skin Physiology"
- Murad, H. "Pregnancy and Skin Care: Wait Till the Baby is Born"
- Murad, H. "Skin Reactions: An Explanation of Contact Dermatitis"

Murad, H. "How to Improve Your Relationship with the Dermatologist"

American Academy of Dermatology Annual Meeting – Cosmetics and use of AHA's, December 1991

"Update on Alpha Hydroxy Acids," Cosmetic Peel Workshop, June 1993

"The Latest Advances in Cosmetic Surgery of the Face", The Foundation for Plastic Surgery, August 1993

"Alpha Hydroxy Acids and Glycolic Acid Peels", San Diego, Cosmetic Dermatology Meeting, October 1993

"Glycolic Acid peeling, Glycolic Acid Exfoliation", Aspers, January 1994

"How do Acne and Glycolic Acid Go Hand in Hand", Chicago Cosmetologists Association, April 1994

"Glycolic Acid and TCA Technique for Crows Feet", Cosmetic Eyelid Rejuvenation Symposium, Nassau, April 1994

Glycolic Acid Peels workshop, and panel member. "Management of Skin Texture", American Academy of Facial Plastic and Reconstructive Surgery, May 1994

"Chemical Peeling and Exfoliation Procedures", Aesthetics Expo '94 Canada, May 1994

"Environmental Aging", I/SPA Palm Springs, August 1994

"Unique Problems and Benefits Associated with Alpha Hydroxy Acids Around the Eyelid Complex – Eyelid Glycolic Acid Peels", Cosmetic Eyelid Rejuvenation Symposium, Beverly Hills, December 1994

Murad, H, The Nails: Their Function and Care", Dermascope, May 1994

"Environmental Aging of the Skin", Current Issues in Women's Health, Sacramento, February 1995

Murad, H, The Use of Glycolic Acid as a Peeling Agent, Dermatologic Clinics, April 1995

Murad, H, Indications, Techniques, Complications, and Alternatives to Chemical Peels of the Eyelids and Periorbital Area. Principles and Practice of Ophthalmic Plastic and Reconstructive Surgery, April 1995

Murad, H, Exercise and the Skin, Dermascope, December 1995

Murad, H, Integrating Medicine and Esthetics, Skin Inc., August 1998

Murad, H, Health, Beauty and the Spa, American Spa, May 2000

Murad, H, Blending Ancient Wisdom and Modern Science, Soap & Cosmetics, October 2000

Murad, H, Tabibian, P, The Effect of an Oral Supplement containing Glucosamine, Amino acids, Mineral, and Antioxidants on Cutaneous Aging: A Preliminary Study, The Journal of Dermatological Science, March 2001

"Internal Approach to Anti-Aging", Society of Plastic Surgical Skin Care Specialists, New York, NY, May 2001

"Advanced Skin Conditions", Institute of Advanced Clinical Esthetics, Seattle, WA, July 2001

Murad, H, Shellow, W, Pomegranate Extract Both Orally Ingested and Topically Applied to Augment the SPF of Sunscreens, Cosmetic Dermatology, October 2001

Murad, H, Ingredient Review, Skin Inc., October 2001

Murad, H, Environmental Aging and the Pomegranate, Les Nouvelles Esthetiques, October 2001

Murad, H. The Inclusive Spa, Les Nouvelles Esthetiques, February 2002

Murad, H, The Power of Zinc, Skin Inc., November 2002

Murad, H, Lange, D., The Murad Method, published by St. Martin's Press, April 2003

Murad, H, Menopause: Unveiling the Mystery, Dermascope, July 2003

KEYNOTE ADDRESSES

Skincare for Today's Environment – Les Nouvelles Esthetiques, Miami, Nov. 1998

Internal Approach to Anti-Aging – May 1999

The Inclusive Spa – International Spa Conference, Las Vegas, Nov. 2000

Skin Types and Conditions – International Beauty Show, Los Angeles, Jan. 2001

New Trends in Dermatology – International Beauty Show, Los Angeles, Jan. 2002

The Inclusive Spa – Cosmoprof, Hong Kong, Nov. 2002

Internal Supplements for Reducing Wrinkles – Noah Worcester Society – Miami, Jan. 2003

Treatments for Anti-Aging – UCI, Irvine CA, May 2003

Treatments for Anti-Aging – Cosmoprof, Las Vegas, June 2003

Internal Supplements for Reducing Wrinkles and Increasing SPF – UCLA, Aug. 2003

Cosmeceutical Trends in the Department Store Arena – IGDS, Tokyo, Japan, Sept 2003

Cosmeceuticals, Nutraceuticals, Technoceuticals – LifeFest Maui, Sept. 2003

PATENTS:

1. **U.S. Patent No. 5,804,168** issued on September 8, 1998: a pharmaceutical formulation for advantageously protecting skin damage caused by UV sources such as sun. This formula may be used alone or in conjunction with a sunscreen to provide protection from UV light. This is our Environmental Shield nutritional supplement.
2. **U.S. Patent No. 5,804,594** issued on September 8, 1998: a formulation for the reduction of wrinkles and the improvement of other skin conditions such as skin elasticity and skin

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softness. The prevention and treatment of unhealthy skin such as aged skin or skin overexposed to sunlight may be accomplished. This is our Youth Builder nutritional supplement.

3. **U.S. Patent No. 5,962,517** issued on October 5, 1999: a pharmaceutical composition for treating acne and conditioning the skin cells. This is our Pure Skin nutritional supplement.
4. **U.S. Patent No. 5,972,999** issued on October 26, 1999: same as 5,804,594 except for the removal of Catechin and the inclusion of the invention for topical use. This is Murad's Co-3 formula.
5. **U.S. Patent No. 6,071,541** issued on June 6, 2000: a formulation for the prevention, treatment and management of skin conditions such as Seborrheic Dermatitis, Psoriasis, Folliculitis, Rosacea, Perioral Dermatitis, Acne and other inflammatory skin conditions. This invention is Acne Prone formula.
6. **U.S. Patent No. 6,194,452** issued on February 27, 2001: a pharmaceutical composition for the delivery of stabilized, non-irritating vitamin C for the treatment of skin damage caused by free radicals. This is Daily Renewal Complex.
7. **U.S. Patent No. 6,207,694** issued on March 27, 2001: a pharmaceutical composition for managing dandruff, eczema, hair thinning, irritation, psoriasis and seborrhea. This technology is incorporated into dandruff and thinning hair products.
8. **U.S. Patent No. 6,271,246** issued on August 7, 2001: a pharmaceutical composition for managing dandruff, eczema, hair thinning, irritation, psoriasis and seborrhea. This technology is incorporated into dandruff and thinning hair products.
9. **U.S. Patent No. 6,296,880** issued on October 2, 2001: An antiviral skin cleansing pharmaceutical composition.
10. **U.S. Patent No. 6,358,539** issued on March 19, 2002: A composition and method for reducing or eliminating the appearance of cellulite.
11. **U.S. Patent No. 6,383,523** issued on May 7, 2002: An antifungal skin cleansing pharmaceutical composition.
12. **U.S. Patent No. 6,515,007** issued on February 4, 2003: a pharmaceutical composition for managing dandruff, eczema, hair thinning, irritation, psoriasis and seborrhea. This technology is incorporated into dandruff and thinning hair products.
13. **U.S. Patent No. 6,630,163** issued on October 7, 2003: a pharmaceutical composition for managing dermatological conditions having pomegranate as an ingredient together with a hydrophilic moisturizing agent, a hydrophobic moisturizing agent and a hydroxy acid.
14. **U.S. Patent No. (awaiting patent number)**

SOCIETY MEMBERSHIPS:

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American Academy of Dermatology
American Society of Dermatologic Surgery
American Medical Association
Los Angeles Metropolitan Dermatologic Society
California Medical Association
Los Angeles County Medical Association
Pacific Dermatology Society
Noah Worcester Society

TEACHING APPOINTMENTS:

Assistant Clinical Professor of
Dermatology, UCLA

HOSPITAL AFFILIATIONS:

VA Hospital
UCLA Hospital
Daniel Freeman Hospital
Centinela Hospital

AWARDS / RECOGNITIONS:

Crystal Award for Contributions and Commitment to the Esthetics Industry, by the International Congress of Esthetics, Nov. 2000

Premiere Golden Star Awarded to Dr. Howard Murad on behalf of Big Sisters of Los Angeles, June 2000

Dr. Howard Murad recognized as one of the top 4 Dermatologists in the U.S. -
Vogue Magazine, Aug. 2001

Editors Choice Award, Best Exfoliating Body Cleanser - Allure Magazine, Oct. 2002

Humanitarian Award, for Development of the Murad After School Program - June 2003

Editors Choice Award, Best Acne Body Wash - Day Spa Magazine, Dec. 2003

Best of Wellness Award - Murad Wellness Day, Dec. 2003

PHILANTHROPY

Dr. Murad continually supports many philanthropic efforts and is actively involved with Vista Del Mar Childcare Center, Big Sisters of Los Angeles, the Jewish Community Center of Los Angeles and the Manhattan Beach Roundhouse; a Center for Aquatic Education

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